Appendix B: The Pending Claims

To facilitate the Examiner's review of the patentability of the present invention, Applicant has reproduced below the presently pending claims.

28. **[Three Times Amended]** A method of producing a cross-over protein that contains at least one peptide segment whose sequence is derived from a first protein, and at least one peptide segment whose sequence is derived from a second protein, wherein said second protein has an amino acid sequence that is different from that of said first protein, and wherein each of said peptide segments possesses an N-terminal amino acid residue and a C-terminal amino acid residue, said method comprising:

ligating under chemoselective chemical ligation conditions (i) at least one peptide segment comprising a functional protein module derived from said first protein, and (ii) at least one peptide segment comprising a functional protein module derived from said second protein, wherein each of said peptide segments exhibit sufficient homology to a functional domain of a chemokine, macrophage migration inhibitory factor, cytokine, trefoil peptide, growth factor, protease inhibitor, or protein toxin, to permit said peptide segments to mediate the function of said functional domain when incorporated into said cross-over protein, wherein the C-terminal residue of said peptide segment derived from said first protein and the N-terminal residue of said peptide segment derived from said second protein comprise compatible reactive groups capable of chemoselective chemical ligation to one another, whereby a covalent bond is formed between said compatible reactive groups of said peptide segments so as to produce a chemical ligation product comprising a cross-over protein in which the C-terminal residue of the peptide segment derived from said first protein is ligated to the N-terminal residue of said peptide segment derived from said second protein; wherein said first and

second proteins are jointly selected from the group consisting of chemokines, macrophage migration inhibitory factors, cytokines, trefoil peptides, growth factors, protease inhibitors, and protein toxins.

29. **[Twice Amended]** The method of claim 28 further comprising the step of conducting one or more additional ligations with one or more additional peptide segments, each possessing an N-terminal amino acid residue and a C-terminal amino acid residue, wherein each of said one or more additional peptide segments exhibit sufficient homology to a functional domain of a chemokine, macrophage migration inhibitory factor, cytokine, trefoil peptide, growth factor, protease inhibitor, or protein toxin, to permit said peptide segments to mediate the function of said functional domain when incorporated into said cross-over protein, wherein said additional peptide segments are selected from the group consisting of a peptide whose C-terminal residue comprises a reactive group capable of chemoselective chemical ligation with a reactive group of an N-terminal residue of another peptide, and a peptide whose N-terminal residue comprises a reactive group capable of chemoselective chemical ligation with a reactive group of an C-terminal residue of another peptide.

30. **[Three Times Amended]** The method of claim 28, wherein the first and second protein molecules from whose sequences said peptides are derived are chemokine protein molecules.

31. **[Amended]** The method of claim 28, wherein said chemoselective chemical ligation is selected from the group consisting of native chemical ligation, oxime forming chemical ligation, thioester forming ligation, thioether forming ligation, hydrazone forming ligation, thiazolidine forming ligation, and oxazolidine forming ligation.

32. **[Three Times Amended]** A method of producing a cross-over protein library whose members contain two or more peptide segments, wherein each of said peptide segments exhibit sufficient homology to a functional domain of a chemokine, macrophage migration inhibitory factor, cytokine, trefoil peptide, growth factor, protease inhibitor, or protein toxin, to permit said peptide segments to mediate the function of said functional domain when incorporated into said cross-over protein, each segment possessing an N-terminal amino acid residue and a C-terminal amino acid residue, and wherein the peptide segments of said members are derived from two or more different proteins, said method comprising:

incubating under chemoselective ligation reaction conditions a plurality of unique peptide segments each comprising one or more functional protein modules derived from a member of a first set of protein molecules and a plurality of unique peptide segments each comprising one or more functional protein modules derived from a member of a second set of protein molecules wherein the C-terminal residues of each of said peptide segments derived from said members of said first set of protein molecules and the N-terminal residue of each of said peptide segments derived from said members of said second set of protein molecules comprise compatible reactive groups capable of chemoselective chemical ligation to one another, whereby a covalent bond is formed between said compatible reactive groups of said peptide segments so as to produce a plurality of chemical ligation products comprising a plurality of unique cross-over proteins, wherein, for each such cross-over protein, the C-terminal residue of a peptide segment derived from a member of said first set of protein molecules is ligated to the N-terminal residue of a peptide segment derived from a member of said second set of protein molecules; wherein said first and second proteins are jointly selected from the group consisting of chemokines, macrophage migration

inhibitory factors, cytokines, trefoil peptides, growth factors, protease inhibitors, and protein toxins.

33. **[Three Times Amended]** The method of claim 32, wherein said first and second set of proteins from whose sequences said peptides are derived are chemokine protein molecules.

34. **[Three Times Amended]** The method of claim 32, wherein said first and second set of proteins from whose sequences said peptides are derived are cytokine protein molecules.

35. **[Four Times Amended]** The method of claim 28, wherein the first and second protein molecules from whose sequences said peptides are derived are cytokine protein molecules.

36. The method of claim 32, wherein said chemoselective chemical ligation is selected from the group consisting of native chemical ligation, oxime forming chemical ligation, thioester forming ligation, thioether forming ligation, hydrazone forming ligation, thiazolidine forming ligation, and oxazolidine forming ligation.